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Major Article

Phage Therapy as an Approach to Control *Salmonella enterica* serotype Enteritidis Infection in Mice

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Abstract

Introduction: *Salmonella enterica* serotype Enteritidis (*S.* Enteritidis) is a cause of food-borne human illness. Given the prevalence of antibiotic resistance of *Salmonella* Enteritidis and the lack of antibiotic efficacy in future years, its replacement with other agents is necessary. One of the most useful agents is bacteriophages. **Methods**: *S.* Enteritidis was identified using a multiplex polymerase chain reaction assay. The effective bacteriophages were isolated from hospital wastewater samples. The effects of the bacteriophages were evaluated both *in vitro* and *in vivo*. **Results**: The phage SE20 belonged to the Podoviridae family, and the genome size was 40 kb. The evaluation of phage SE20 at variable pH ranges showed its susceptibility to pH < 3 and pH > 12. The animal model showed that mice infected with *S.* Enteritidis developed hepatomegaly and splenomegaly, but did not experience gastrointestinal complications after receiving the bacteriophages. **Conclusions**: The results of this study suggest that phage SE20 is a promising candidate for controlling salmonellosis caused by *Salmonella* Enteritidis.

Keywords: *Salmonella enterica* serotype Enteritidis. Phage SE20. Pulsed-field gel electrophoresis. Mice. Sewage.

INTRODUCTION

Foodborne diseases are one of the most important economic and health problems in industrialized and developing countries. In recent years, *Salmonella* has been one of the most common causes of foodborne diseases[1]. Salmonellosis is an infectious disease that is often transmitted through contaminated food, especially food products derived from meat, chicken, eggs, animal feed, milk, and sometimes vegetables[2,3]. However, estimating the prevalence of salmonellosis is challenging in developing countries, as no comprehensive research has been conducted in this area[4-8]. In addition, non-typhoidal salmonellosis is a disease caused by *Salmonella* serotypes other than Typhi, Paratyphi A, Paratyphi B, and Paratyphi C. Numerous studies have been carried out globally on the prevalence of *Salmonella* serotypes in different regions[9-11]. *Salmonella enterica* subsp. *enterica* serovar Enteritidis and Typhimurium are two common serotypes that have been identified in Iran and other countries[12-15].

Over the past two decades, the prevalence of antibiotic-resistant *Salmonella* has become a serious global challenge. Moreover, the extensive use of antibiotics, for instance, as a standard component of domestic animal feed, has led to antibiotic resistance[16]. In recent years, multidrug-resistant (MDR) strains have become major global concerns, and many studies in Iran and other countries have reported the high resistance of *Salmonella* strains to several antibiotics[9,22]. Antibiotics are among the most commonly used drugs in human medicine and are used unnecessarily for up to 50% of

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